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L1 0 S XLKCYTCKQPMTSAAC/SQEP
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L4 0 S QLKCYTCKQPMTSAAC/SQEP
L5 0 S XLKCYTCKXPMTSAAC/SQEP

FILE 'CA' ENTERED AT 15:13:31 ON 20 AUG 1998
L6 16 S (ANTINEOPLASTIC PROTEIN OR ANUP)/BI,AB

=> d 1-16 bib,ab

L6 ANSWER 1 OF 16 CA COPYRIGHT 1998 ACS
AN 127:306448 CA
TI In vitro and in vivo antitumor activity of a plasma cytokine identical to antineoplastic urinary protein: tumor cell killer protein (TCKP, p 32)
AU Sloane, N. H.; Davis, L. H.
CS Department of Biochemistry, Department of Microbiology and Molecular Cell Sciences, University of Tennessee, University of Memphis, Memphis, TN, 38163, USA
SO Tumor Targeting (1996), 2(5/6), 322-326
CODEN: TUTAF9; ISSN: 1351-8488
PB Chapman & Hall
DT Journal
LA English
AB A homogeneous protein with a mol. wt. of 32 kDa was isolated from human plasma. This protein is chem., immunol. and biol. equiv. to the antineoplastic urinary protein previously isolated from human urine and later found to be present in 5% of human granulocytes. The amino acid sequence of the N-terminal end of the cytokine has been shown to be unique. The plasma cytokine (in the form of a Florisil eluate) caused regression in two human tumor cell lines implanted in nude mice. The biol. activity of the cytokine and the N-terminal nonapeptide could be related to a conformational change in the protein and peptide occurring in the presence of SDS.

L6 ANSWER 2 OF 16 CA COPYRIGHT 1998 ACS
AN 127:75634 CA
TI Activation of NF-.kappa.B by antineoplastic agents. Role of protein kinase C
AU Das, Kumuda C.; White, Carl W.
CS Dep. Pediatrics, National Jewish Medical Res. Center, Denver, CO, 80206, USA
SO J. Biol. Chem. (1997), 272(23), 14914-14920
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Paclitaxel can induce tumor necrosis factor (TNF) and interleukin-1 gene expression, similar to lipopolysaccharides. Since lipopolysaccharide-induced expression of TNF is related to activation of NF-.kappa.B, the authors detd. whether NF-.kappa.B could be activated by paclitaxel. In the human lung adenocarcinoma cell line A549, paclitaxel activated NF-.kappa.B in a dose-dependent manner with maximal activation after 2-4 h. Since paclitaxel could upregulated TNF and interleukin-1 secretion and subsequent NF-.kappa.B activation could be caused by these cytokines, the effect of two other groups of anticancer drugs including vinca alkaloids (vinblastine and vincristine) and anthracyclines (daunomycin and doxorubicin), neither of which induce TNF or interleukin-1 gene expression, were examd. Like paclitaxel, vinblastine, vincristine, daunomycin, and doxorubicin each caused activation of NF-.kappa.B. Therefore, it is unlikely that activation of NF-.kappa.B caused by these agents or by paclitaxel is mediated via cytokine up-regulation. Furthermore, actinomycin D and cycloheximide, inhibitors of transcription and translation, resp., did not inhibit paclitaxel-induced NF-.kappa.B activation. Several other transcription factors such as AP-1, AP-2, CREB, SP-1, or TFIID were not activated by antineoplastic agents, demonstrating specificity of NF-.kappa.B activation. The involvement of both subunits in the NF-.kappa.B DNA binding complex was demonstrated by its abrogation by anti-p65 and by supershift by anti-p50 antibodies. Since protein phosphorylation is implicated in the activation of NF-.kappa.B, the effect of anticancer drugs on protein kinase C activity was measured. Vincristine, daunomycin, and paclitaxel significantly increased protein kinase C activity, and vinblastine and doxorubicin caused similar trends. Following treatment with antineoplastics (1-4 h), cytoplasmic I.kappa.B.alpha. degrdn. occurred concomitantly with translocation of p65 to the nucleus. Specific protein kinase C inhibitors (bisindolylmaleimide (GF109203X) and calphostin C) blocked the activation of NF-.kappa.B by each compd. Hence, protein kinase C activation may contribute to NF-.kappa.B activation by antineoplastic agents.

L6 ANSWER 3 OF 16 CA COPYRIGHT 1998 ACS
AN 124:143279 CA
TI Partial N-terminal amino acid sequence of the anti-neoplastic urinary protein (**ANUP**) and the anti-tumor effect of the N-terminal nonapeptide of the unique cytokine present in human granulocytes
AU Ridge, Richard J.; Sloane, Nathan H.
CS Woods Hole Oceanographic Inst., Woods Hole, MA, 02543, USA
SO Cytokine (1996), 8(1), 1-5
CODEN: CYTIE9; ISSN: 1043-4666
DT Journal
LA English
AB The N-terminal amino acid sequence of the anti-neoplastic urinary protein (**ANUP**), a unique cytokine present in human granulocytes, was detd. to be: Pyroglu-Leu-Lys-X-Tyr-Thr-X-Lys-Glu-Pro-Met-Thr-Ser(Thr)-Ala-Ala...this sequence showed no significant

homol. with any other protein when used in database searches. Furthermore, a synthetic nonapetide corresponding to the first nine residues, with Cyc in positions 4 and 7, was a biol. active in vitro anti-tumor agent. An alternative method for the purifn. of **ANUP** to that previously reported is also presented. This method involves differential Amicon Diaflo membrane filtration.

L6 ANSWER 4 OF 16 CA COPYRIGHT 1998 ACS
AN 121:271544 CA
TI Augmentation of interleukin-6 (IL-6) expression in squamous carcinoma cells and normal human keratinocytes treated with recombinant anti-neoplastic protein (ACP)
AU McKenzie, Roderick C.; Venner, Thomas J.; Sauder, Daniel N.; Farkas-Himsley, Hannah
CS Division Dermatology, University Toronto, Toronto, ON, M4N 3M5, Can.
SO Anticancer Res. (1994), 14(3A), 1165-8
CODEN: ANTRD4; ISSN: 0250-7005
DT Journal
LA English
AB A protein purified from Escherichia coli has previously been shown to have cytotoxic effects on neoplastic cells of several lineages both in vitro and in vivo. Accordingly, this protein has been named anti-neoplastic protein (ACP). Although ACP kills neoplastic cells by inducing apoptosis, it has negligible effects on various normal cells. In addn. to the direct cytotoxic effects of ACP on tumor cells, previous studies have shown that in vivo ACP increase tumoricidal activity of cytotoxic lymphocytes. The authors investigated whether cytokines from host or tumor cells play a part in the enhanced cellular immunity seen in ACP-treated tumor-bearing mice. Growth of normal human keratinocytes (KC) was not affected by subnanogram amts. of ACP, however ACP dose-dependently killed KHT cells, a murine fibrosarcoma cell line (LD50=8.times.104 ng/cell). as well as the human squamous carcinoma cell line COLO-16 (LD50=2.5.times.10-4 ng/cell). Testing purified ACP on cultures of normal keratinocytes and squamous carcinoma cell lines revealed that ACP could induce both mRNA and protein for interleukin-6 (IL-6). MRNA for IL-6 increased dose-dependently 4h after treatment of COLO-16 squamous carcinoma cells with 10-4 to 10-2 ng/cell ACP. Maximal increment was 50-fold. Interleukin-6 message remained elevated up to 24h later in both normal keratinocytes and squamous carcinoma cultures treated with ACP. Conditioned supernates from these cultures were analyzed by ELISA and found to have 4-fold higher levels of IL-6 protein than untreated cells after 4h. After 24h, IL-6 did not increase above the 4h level. Boiling of the ACP prepn. showed that the cytokine induction was not due to contaminating lipopolysaccharide. The cytotoxic effect of ACP on tumor cells in vitro was not due to IL-6 protein induction since neither recombinant IL-6, nor the other proinflammatory cytokines, IL-1.alpha. or tumor necrosis factor-.alpha. (0.1-10ng/mL) were able to kill malignant cells. The authors demonstrated IL-6 gene induction by ACP in the squamous carcinoma lines as well as in normal KC. Thus, the in vivo effectiveness of ACP against tumors may be due to stimulatory effects of IL-6 on host immunity.

11/14/82

L6 ANSWER 5 OF 16 CA COPYRIGHT 1998 ACS
AN 121:26889 CA
TI Partial primary amino acid sequence of the antineoplastic urinary protein, a cytokine present in granulocytes
IN Sloane, Nathan H.
PA USA
SO U.S., 4 pp. Cont. of U.S. Ser. No. 919,885.
CODEN: USXXAM
PI US 5298604 A 940329
AI US 93-116539 930902
PRAI US 92-919885 920727

06/919,885
08/116,539

US 4359415

DT Patent
LA English
AB Electrophoretically homogeneous human antineoplastic urinary protein (**ANUP**) contains a blocked N-terminal amino acid that has been identified as pyroglutamic acid. Removal of the pyroglutamyl residue by the use of pyroglutamyl aminopeptidose results in the formation of the deblocked protein which is also an antineoplastic mol. The amino acid sequence of the deblocked **ANUP** 16 KD monomer showed the following sequence: LKCYTCKEPMT(T/S)AA. **ANUP** was purified from urine by antibody affinity chromatog. **ANUP** is proposed for use as an antitumor substance since it is non-toxic to human cells, specifically inhibits only human cancer cell lines, and causes regression of human tumor cell lines implanted into nude mice.

L6 ANSWER 6 OF 16 CA COPYRIGHT 1998 ACS
AN 116:227789 CA
TI Inhibition of protein kinase C by ether-linked lipids is not correlated with their antineoplastic activity on WehI-3B and R6X-B15 cells
AU Salari, Hassan; Dryden, Peter; Davenport, Ruth; Howard, Sandra; Jones, Kelvin; Bittman, Robert
CS Dep. Med., Univ. British Columbia, Vancouver, BC, V6H 3Z6, Can.
SO Biochim. Biophys. Acta (1991), 1134(1), 81-8
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
AB To test the hypothesis that the action of antineoplastic ether-linked lipids in leukemic cells is assocd. with their ability to inhibit protein kinase C (PKC), the authors have compared the effects of two ether-linked lipids, 1-O-hexadecyl-2-O-methyl-sn-glycero-3-phosphocholine (ET16-OCH3-GPC) and 1-O-hexadecyl-2-O-methyl-sn-glycero-3-(S-.beta.-D-1'-thioglucopyranosyl)-sn-glycerol (ET16-OCH3-.beta.-thio-Glc), on two different leukemic cell lines (WEHI-3B and R6X-B15). ET16-OCH3-GPC killed WEHI-3B cells with an EC50 value of 2.5 .mu.M, whereas it was far less effective against R6X-B15 cells (EC50 = 40 .mu.M). In contrast, the .beta. anomer of ET16-OCH3-.beta.-thio-Glc did not kill either cell line at concns. up to 40 .mu.M. Both ET16-OCH3-GPC and ET16-OCH3-thio-Glc inhibited 12-O-tetradecanoylphorbol 12,13-dibutyrate (TPA)-induced PKC translocation in both WEHI-3B and R6X-B15 cells. When WEHI-3B cells were first exposed to TPA, and then to ET16-OCH3-GPC, no significant decrease in PKC activity in the particulate fraction was noticed. When, however, the cells were first exposed to ET16-OCH3-GPC and then to TPA, the enzyme activity in the particulate fraction was decreased by 20-30%. A phorbol dibutyrate binding assay showed that the decrease in membrane-assocd. PKC activity and the increase in cytosolic PKC activity did not result from impeded enzyme translocation. These results suggest that the similar PKC inhibitory potency of ET16-OCH3-GPC and ET16-OCH3-.beta.-thio-Glc: (a) is not correlated with the widely different cytotoxicities of these agents and (b) is probably due to interference with the binding of diacylglycerol/phosphatidylserine or TPA to PKC. Taken together, these results suggest that the ether-linked lipids compete with diacylglycerol/phosphatidylserine or TPA for binding sites on PKC required for enzyme activation.

L6 ANSWER 7 OF 16 CA COPYRIGHT 1998 ACS
AN 113:227069 CA
TI Analysis of the substrate binding sites of human galactosyltransferase by protein engineering
AU Aoki, Daisuke; Appert, Hubert E.; Johnson, Dennis; Wong, Shan S.; Fukuda, Michiko N.
CS La Jolla Cancer Res. Found., La Jolla, CA, 92037, USA
SO EMBO J. (1990), 9(10), 3171-8

CODEN: EMJODG; ISSN: 0261-4189
DT Journal
LA English
AB An expression vector, pIN-GT, encoding the sol. form of .beta.-1,4-galactosyltransferase (GT) has been constructed from human GT cDNAs and the pIN-III-ompA2 expression vector. Escherichia coli strain SB221 harboring the pIN-GT plasmid produces and secretes a fusion protein consisting of the ompA signal and GT. The expression of GT was detected by assaying enzymic activity as well as by Western blotting using anti-GT antibodies. The recombinant GT was purified to homogeneity by N-acetylglucosamine-Sepharose affinity chromatog. The N-terminal peptide sequence of purified GT confirmed the cleavage site of the fusion protein by bacterial signal peptidase. This expression system was utilized to produce mutant forms of GT in order to identify specific amino acids involved in substrate binding sites. Photoaffinity labeling of GT with UDP-galactose analog, 4-azido-2-nitrophenyluridylylpyrophosphat e (**ANUP**), followed by CNBr cleavage revealed that **ANUP** bound to a fragment of GT composed of amino acid residues from Asp276 to Met328. Within this peptide segment, Tyr284, Tyr287, Tyr309, Trp 310 and Trp312 were sep. substituted by glycine and Tyr287 by phenylalanine by site-directed mutagenesis. Enzymic activity assay showed drastic redn. of the activity in all of the mutants except that Tyr287 .fwdarw. Phe remained as active as wild-type GT. Kinetic studies of the mutated GT showed that Tyr284, Tyr309 and Trp310 are critically involved in the N-acetylglucosamine binding and Tyr309 is involved in UDP-galactose binding as well. These results indicate that these tyrosines and tryptophans in GT are essential for the binding of the acceptor N-acetylglucosamine, and that UDP-galactose also binds to residue(s) nearly where N-acetylglucosamine binds.

L6 ANSWER 8 OF 16 CA COPYRIGHT 1998 ACS
AN 112:113898 CA
TI Purification and characterization of an antibacterial and **antineoplastic protein** secretion of a sea hare, Aplysia juliana
AU Kamiya, Hisao; Muramoto, Koji; Goto, Rina; Sakai, Masahiro; Endo, Yoshio; Yamazaki, Masatoshi
CS Sch. Fish. Sci., Kitasato Univ., Iwate, 022-01, Japan
SO Toxicon (1989), 27(12), 1269-77
CODEN: TOXIA6; ISSN: 0041-0101
DT Journal
LA English
AB The fetid secretion of a sea hare, A. juliana, was lethal to crabs and also inhibited the growth of bacteria. When the secretion was partitioned between water and n-hexane, only the n-hexane layer, which had a nauseating odor, was lethal to crabs. The water-sol. fraction showed strong antibacterial activity and inhibited the growth of both gram-pos. and gram-neg. bacteria. Antibacterial activity of the water-sol. fraction was destroyed by heating at 50.degree. for 15 min, but was resistant to treatment with proteolytic enzymes. The active principle, named julianin-S, was purified by gel filtration and ion exchange chromatog. The purified specimen gave a single protein showing a relative mol. wt. of .apprx.67,000, as detd. by gel filtration. Julianin-S inhibited the growth of Bacillus subtilis by 50% at a concn. of 70 ng protein/mL. It was also cytotoxic to murine tumor cells and inhibited in vitro growth of L1210 cells by 50% at a concn. of 8 ng protein/mL.

L6 ANSWER 9 OF 16 CA COPYRIGHT 1998 ACS
AN 105:110799 CA
TI Phospholipid/calcium-dependent protein kinase (protein kinase C) system: a major site of bioregulation
AU Kuo, J. F.; Shoji, Mamoru; Girard, Peggy R.; Mazzei, Gonzalo J.;

Turner, R. Scott; Su, Huai De
CS Sch. Med., Emory Univ., Atlanta, GA, USA
SO Adv. Enzyme Regul. (1986), 25, 387-400, 7 plates
CODEN: AEZRA2; ISSN: 0065-2571
DT Journal; General Review
LA English
AB A review with 49 refs., of regulatory aspects of the protein kinase C (I) system. The substrate specificity determinants of I as probed with synthetic peptide substrates and inhibitors, esp. those related to myelin basic protein, and the I system in leukemic cells and its inhibition by anticancer agents and stimulation by tumor promoters are discussed.

L6 ANSWER 10 OF 16 CA COPYRIGHT 1998 ACS
AN 105:3411 CA
TI Radiometric evaluation of antibacterial activity of bouvardin (NSC 259968) on Escherichia coli and Staphylococcus aureus
AU Basrur, V. S.; Chitnis, M. P.; Menon, R. S.
CS Cancer Res. Inst., Tata Mem. Cent., Bombay, 400 012, India
SO Indian J. Exp. Biol. (1986), 24(3), 156-8
CODEN: IJEBA6; ISSN: 0019-5189
DT Journal
LA English
AB Bouvardin, a cyclic hexapeptide and a new **antineoplastic protein** synthesis inhibitor, was studied for its effects on bacterial growth and metab. E. coli And S. aureus as representative types of gram-neg. and gram-pos. bacteria, resp., were used for these studies. Garamycin and kanamycin were also employed as known antibiotics to compare their effects with bouvardin. Both garamycin and kanamycin markedly reduced [14C]glucose metab. at a concn. of 10 .mu.g/mL. However, bouvardin revealed no such antibacterial activity in these microorganisms.

L6 ANSWER 11 OF 16 CA COPYRIGHT 1998 ACS
AN 104:102121 CA
TI Studies on antineoplastic fraction from human urine. Characterization of the major protein in this fraction
AU Sloane, Nathan H.; Lynn, W. R.; Macleod, R. M.; Hade, E. P. K.; Pottathil, Raveendran; Kyriazis, Andreas P.
CS Coll. Med., Univ. Tennessee, Memphis, TN, 38163, USA
SO Biochem. J. (1986), 234(2), 355-62
CODEN: BIJOAK; ISSN: 0306-3275
DT Journal
LA English
AB A fraction from human urine which exhibits antiproliferative activity against human tumor cell lines without affecting the growth of several normal diploid cell lines or tumor cells of mouse of hamster origin was isolated. The major protein present in this fraction was characterized and tentatively designated antineoplastic urinary protein (**ANUP**). An s020,w value of 3.69 S, and a subunit mol. mass of 16,300 dalton. Centrifugation data also indicated that the protein self-assocs. The amino acid anal. of **ANUP** was consistent with its low pI (4.2). Furthermore, the amino acid compn. exhibited some features similar to collagen, as shown by high levels of proline and glycine, the absence of cysteine, and the presence of low levels of hydroxyproline.

L6 ANSWER 12 OF 16 CA COPYRIGHT 1998 ACS
AN 102:178807 CA
TI Inhibition of phospholipid/calcium dependent protein kinase and phosphorylation of leukemic cell proteins by CP-46,665-1, a novel antineoplastic lipoidal amine
AU Shoji, Mamoru; Vogler, William R.; Kuo, J. F.
CS Sch. Med., Emory Univ., Atlanta, GA, 30322, USA
SO Biochem. Biophys. Res. Commun. (1985), 127(2), 590-5

CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB CP 46665-1 (I) [72618-10-1] inhibited phospholipid/Ca2+-dependent protein kinase [9026-43-1] (PL/Ca-PK, or protein kinase C) in a human leukemic cell line, with an IC50 (concn. causing a 50% inhibition) of 10 .mu.M. Its inhibition of the enzyme was reversed by phosphatidylserine, but not by Ca2+. The agent also inhibited the enzyme activity which was further augmented by 12-O-tetradecanoylphorbol-13-acetate (TPA), mezerein or diolein. Phosphorylation of endogenous proteins from HL-60 cells by the enzyme, with or without being further augmented by TPA, was inhibited by I as well as by alkyllysophospholipid (an antineoplastic agent). I, while without effect on cyclic AMP-dependent protein kinase, also inhibited myosin light chain kinase (a calmodulin/Ca2+-dependent protein kinase). Apparently, inhibition of the Ca2+-effector enzymes may be related in part to the antimetastatic activity of the lipoidal amine.

L6 ANSWER 13 OF 16 CA COPYRIGHT 1998 ACS
AN 100:2721 CA
TI Photoaffinity labeling of lactose synthase with a UDP-galactose analog
AU Lee, Timothy K.; Wong, Lee Jun C.; Wong, Shan S.
CS Dep. Chem., Univ. Lowell, Lowell, MA, 01854, USA
SO J. Biol. Chem. (1983), 258(21), 13166-71
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB A photoaffinity analog of UDP-galactose, 4-azido-2-nitrophenyluridylyl pyrophosphate (**ANUP**), was synthesized for the investigation of the binding topog. of .alpha.-lactalbumin on galactosyltransferase from bovine milk. Results obtained from steady-state kinetics show that **ANUP** is an effective competitive inhibitor against UDP-galactose in lactose and N-acetyllactosamine synthases. The specific binding of **ANUP** to the UDP-galactose-binding site is further demonstrated by its ability to facilitate the formation of the lactose synthase complex on solid supports, either alone or in the presence of glucose or N-acetylglucosamine. **ANUP** inactivates galactosyltransferase on irradn. One mol of **ANUP** was incorporated per mol of enzyme inactivated. This process is Mn2+ dependent and can be prevented by UDP-galactose. Glucose and N-acetylglucosamine render only partial protection. Photoaffinity labeling of lactose synthase either free in soln. or immobilized on Sepharose does not result in any redn. of the .alpha.-lactalbumin modifier activity. In addn., no incorporation of radioactivity into .alpha.-lactalbumin was obsd. when radioactive **ANUP** was used, whereas galactosyltransferase was labeled. Apparently, .alpha.-lactalbumin does not bind to galactosyltransferase in the region of the **ANUP** site, suggesting that the location of protein-protein interaction between the 2 subunits of lactose synthase may be removed from the UDP-galactose-binding domain.

L6 ANSWER 14 OF 16 CA COPYRIGHT 1998 ACS
AN 96:149077 CA
TI Spectral studies of actinoxanthine in its active form
AU Pletnev, V. Z.; Starovoitova, N. V.; Chupova, L. A.; Efremov, E. S.
CS M. M. Shemyakin Inst. Bioorg. Chem., Moscow, USSR
SO Bioorg. Khim. (1982), 8(2), 169-71
CODEN: BIKHD7
DT Journal
LA Russian
AB UV spectroscopic, fluoroscence, and CD spectral characteristics of the chromophore of **antineoplastic protein**-type

antibiotic actinoxanthine (I) [59680-34-1] in active form were compared with the corresponding chromophore of a homologous holoprotein neocarzinostatin (II) [9014-02-2]. For example, the holo form of I compared to the apo form was different in its UV absorption in the 300-370 nm region. The chromophore of II had an absorption in the 320-380 nm region. The presence of a naphthalenecarboxylic acid chromophore was presumably responsible for the absorption in this region. The absorption at .apprx.280 nm was probably due to the arom. portion of the protein. The emission spectrum of I showed fluorescence with max. at 420 nm. I had relatively higher ellipticity in the CD spectrum in the arom. region (280-300 nm) compared to II.

L6 ANSWER 15 OF 16 CA COPYRIGHT 1998 ACS
AN 88:110435 CA
TI Cesalin - an anti-neoplastic protein
AU Montgomery, Rex; Yamauchi, Fumio; Bradner, William T.
CS Dep. Biochem., Univ. Iowa, Iowa City, Iowa, USA
SO Lloydia (1977), 40(3), 269-74
CODEN: LLOYA2; ISSN: 0024-5461
DT Journal
LA English
AB An **antineoplastic protein** was isolated from the endosperm of the seeds of Caesalpinia gilliesii by extn. with water, dialysis and pptn. by (NH4)2SO4 or acidification. The pptd. protein mixt. was sepd. by column chromatog. into 3 principal proteins, one of which, termed cesalin (I), inhibited the growth of Walker 256 carcinosarcoma. There was an assocd. carbohydrate with I that could be largely removed by chromatog. on hydroxylapatite; the remaining carbohydrate (about 3%) was a hexosan. I, mol. wt. 110,000, migrated as a single component inby polyacrylamide gel electrophoresis at pH 8.3, but in a denaturing system contg. sodium dodecyl sulfate, 3 bands were obsd. These corresponded to protein sub-units of approx. 30,000 daltons. Antitumor tests in rats showed 70-80% inhibition of Walker 256 carcinosarcoma growth at a dose of 80 .mu.g cesalin/kg/day.

L6 ANSWER 16 OF 16 CA COPYRIGHT 1998 ACS
AN 80:55843 CA
TI Effect of 5-fluorouracil and fluorafur on some aspects of protein metabolism
AU Sal'nik, B. Yu.; Bakhareva, G. I.; Telesheva, V. A.
CS USSR
SO Vop. Radiobiol. Biol. Deistviya Tsitostatich. Prep. (1972), 4, 57-62
From: Ref. Zh., Biol. Khim. 1973, Abstr. No. 6F2134
DT Journal
LA Russian
AB The effects of a single i.p. injection of 5-fluorouracil [51-21-8] or fluorafur [316-46-1] on the contents of DNA and of protein and residual N in the spleen, liver, and myocardium of rats differed somewhat from those after a 10-day course of daily, oral doses. A single administration of 5-fluorouracil decreased the protein N (most markedly in the liver), the residual N, and the DNA. Protein N decreased following oral treatment with 5-fluorouracil. The effects of fluorafur were less pronounced than those of 5-fluorouracil, and DNA content did not change significantly.

=> file biosis, medline, embase, uspatful, wpids

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     FILE 'REGISTRY' ENTERED AT 14:58:06 ON 20 AUG 1998
L1             0 S XLKCYTCKQPMTSAAC/SQEP
L2             0 S XLKCYTCKEPMTSAAC/SQEP
L3             0 S (ANTINEOPLASTIC PROTEIN OR ANUP)/CN
L4             0 S QLKCYTCKQPMTSAAC/SQEP
L5             0 S XLKCYTCKXPMTSAAC/SQEP

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L6            16 S (ANTINEOPLASTIC PROTEIN OR ANUP)/BI,AB

     FILE 'BIOSIS, MEDLINE, EMBASE, USPATFULL, WPIDS' ENTERED AT
     15:20:41 ON 20 AUG 1998

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L7            41 L6

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FULL ESTIMATED COST                                     5.28     109.49

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                                                       ENTRY    SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-15.68

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L9 30 DUP REM L7 (11 DUPLICATES REMOVED)

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L9 ANSWER 1 OF 30 MEDLINE
AN 1998194100 MEDLINE
DN 98194100
TI [Relationship between activity of atrial natriuretic peptide and process of myocardial remodelling in patients with cardiac failure]. Sviaz' aktivnosti predserdnogo natriiureticheskogo peptida i protsessov remodelirovaniia miokarda u bol'nykh s serdechoi nedostatochnost'iu.
AU Fushtei I M; Berezin A E
SO KLINICHESKAIA MEDITSINA, (1998) 76 (1) 11-4.
Journal code: KW2. ISSN: 0023-2149.
CY RUSSIA: Russian Federation
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
EM 199807
EW 19980702
AB Echocardioscopy in M- and B-modes with measurement of routine parameters of central hemodynamics and thickness of carotid intimal-medial segment as well as radioimmunoassay of plasma concentrations of atrial natriuretic peptide (**ANUP**) were performed in 159 patients aged 42-63 years (17 healthy subjects and 142 patients with cardiac failure associated with ischemic heart disease and sinus rhythm, without history of myocardial infarction). The results were indicative of possible use of **ANUP** as a marker of initial cardiac insufficiency and a corrector of the disease prognosis.

L9 ANSWER 2 OF 30 USPATFULL
AN 97:55451 USPATFULL
TI Walk-behind self-propelled multi-functional nursery device
IN Meyer, Thomas A., 1609 Hobe Rd., Woodstock, IL, United States 60098

PI US 5642677 970701
AI US 95-579101 951227 (8)
DT Utility
EXNAM Primary Examiner: Melius, Terry Lee; Assistant Examiner: Pezzuto, Robert
LREP Perrone, Jr., Mathew R. P.
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 760
AB A walk-behind, multi-functional device for use in a nursery is capable cultivating while applying fertilizer and herbicide as desired. An electric clutch assembly combines with a steering assembly to permit easy maneuverability of the walk-behind device.

L9 ANSWER 3 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 97:159998 BIOSIS
DN 99459201
TI Mechanism of increased sensitivity to etoposide in a mitomycin C-resistant human bladder cancer cell line.
AU Xia H; Bleicher R J; Gupta V; Zaren H A; Singh S V
CS Cancer Res. Lab., Mercy Hosp., 1400 Locust St., Pittsburgh, PA 15219, USA
SO International Journal of Cancer 70 (5). 1997. 606-611. ISSN: 0020-7136
LA English
AB The mechanism of increased sensitivity to etoposide (VP16) in a human bladder cancer cell line (182/MMC-2), which is gt 9-fold more resistant to mitomycin C (MMC) compared with parental cells (J82/WT), was investigated. Colony formation assays, following 1 hr drug exposure, revealed that about a 2.2-fold higher concentration of VP-16 was required to kill 50% of the J82/WT cell line compared with J82/MMC-2. The MTT assays, following continuous drug exposure, also showed that the J82/MMC-2 cell line was significantly more sensitive to VP-16 compared with J82/WT. Accumulation of VP-16 was significantly higher in the J82/MMC-2 cell line compared with J82/WT at every drug concentration tested. Likewise, intracellular VP-16 retention was significantly higher in the J82/ MMC-2 cell line compared with J82/WT when drug uptake was measured as a function of varying incubation time and at a fixed VP-16 concentration. The efflux of VP-16 from the J82/MMC-2 cell line was equivalent to that from J82/WT. In agreement with the results of drug uptake studies, the levels of VP-16-induced protein-DNA complexes were markedly higher in the J82/MMC-2 cell line compared with J82/WT. The catalytic activity of topoisomerase II (topo II) in 0.35 M NaCl nuclear extract of J82/WT cells was equivalent to that of J82/MMC-2. The levels of topo II mRNA were also comparable in these cells. Our results suggest that the mechanism responsible for the collateral sensitivity of the J82/MMC-2 cell line to VP-16 may be attributable to a relatively higher drug accumulation in this cell line compared with parental cells.

L9 ANSWER 4 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 97:160289 BIOSIS
DN 99459492
TI Tamoxifen activates cellular phospholipase C and D and elicits protein kinase C translocation.
AU Cabot M C; Zhang Z-C; Cao H-T; Lavie Y; Giuliano A E; Han T-Y; Jones R C
CS John Wayne Cancer Inst. Saint John's Hosp. Health Cent., 2200 Santa Monica Blvd., Santa Monica, CA 90404, USA
SO International Journal of Cancer 70 (5). 1997. 567-574. ISSN: 0020-7136
LA English
AB The antiestrogen tamoxifen is widely used for endocrine therapy of

breast cancer, however, the mechanisms of estrogen receptor-independent interactions of tamoxifen remain ill defined. Here we examine the effect of tamoxifen on the initial steps of cell signal transduction. To this end, phospholipid metabolism and protein kinase C (PKC) translocation were assessed in CCD986SK human mammary fibroblasts treated with tamoxifen. The addition of tamoxifen resulted in dose-dependent and time-dependent increases in the cellular second messengers phosphatidate (PA) and diacylglycerol (DG). On addition of ethanol to the medium, tamoxifen induced the formation of phosphatidylethanol, demonstrating that tamoxifen activates phospholipase D (PLD). Cellular tamoxifen also activates phospholipase C (PLC). In cells prelabeled with choline and ethanolamine, tamoxifen caused increases in choline, phosphorylcholine, ethanolamine and phosphorylethanolamine. Structure-activity relationship studies for activation of PLD revealed that tamoxifen was the most effective, whereas 4-hydroxy tamoxifen was nearly devoid of activity. Phorbol diesters also activated PLD, but estrogen had no influence. Pretreatment of cells with phorbol dibutyrate (PKC down-regulation protocol) blocked phorbol diester- and tamoxifen-induced PLD activity. Exposure of cells to the PKC inhibitor GF 109203X diminished tamoxifen-induced PLD activity. Addition of tamoxifen to cultures elicited selective membrane association of PKC E. We conclude that tamoxifen exerts considerable extra-nuclear influence at the transmembrane signaling level. These events may contribute to effects beyond the scope of estrogen receptor-dependent actions.

L9 ANSWER 5 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 96:440217 BIOSIS
DN 99162573
TI Control of pharmacokinetic profiles of drug-macromolecule conjugates.
AU Takakura Y; Mahato R I; Nishikawa M; Hashida M
CS Dep. Drug Delivery Res., Fac. Pharm. Sci., Kyoto Univ., Sakyo-ku, Kyoto 606-01, Japan
SO Advanced Drug Delivery Reviews 19 (3). 1996. 377-399. ISSN: 0169-409X
LA English

L9 ANSWER 6 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 96:424302 BIOSIS
DN 99155358
TI Biological activity of 26-succinylbryostatin 1.
AU Bignami G S; Wagner F; Grothaus P G; Rustagi P; Davis D E; Kraft A S
CS Div. Hematol./Oncol., Univ. Ala., Birmingham, AL 35294, USA
SO Biochimica et Biophysica Acta 1312 (3). 1996. 197-206. ISSN: 0006-3002
LA English
AB Bryostatin 1, a macrocyclic lactone, has undergone phase I trials as an anticancer agent. Because of the lipid solubility of this compound it must be delivered either in ethanol or in a PET formulation. During the trial, these vehicles caused a large number of treatment-related side effects. We have synthesized the triethanolamine salt of 26-succinylbryostatin 1 and find that this compound is approx. 100-fold more water soluble than bryostatin 1. Because of the potential for clinical use, we have evaluated the biologic activity of this compound. We find that in a concentration-dependent manner 26-succinylbryostatin I is capable of activating protein kinase C (PKC) in vitro and displacing (3H)PDBu from PKC. However, at all concentrations tested the activity was less than the parent compound bryostatin 1. Addition of bryostatin I but not 26-succinylbryostatin 1 to U937 leukemic cells in culture stimulated a drop in cytosolic levels of PKC, addition to U937 cells activated transcription from an AP-1 enhancer construct and c-Jun protein phosphorylation in a PKC, secondary to translocation of PKC to the membrane. Although 26-succinylbryostatin 1 did not stimulate a

drop in the cytosolic aggregation of human platelets. Although injection of bryostatin- I into mice carrying B 16 melanoma inhibits tumor growth, there was no significant inhibition of melanoma growth when identical doses of 26-succinylbrvostatin I were injected. Therefore, 26-succinylbryostatin 1 shares some but not all of the pharmacologic properties of bryostatin 1. This compound can activate protein phosphorylation without lowering cytosolic levels of PKC.

L9 ANSWER 7 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 96:503874 BIOSIS
DN 99226230
TI Ultrafiltration and subsequent high performance liquid chromatography for in vivo determinations of the protein binding of etoposide.
AU Liliemark E; Herngren L; Pettersson B; Peterson C; Liliemark J
CS Dep. Clinical Pharmacol., Karolinska Hosp., Karolinska Inst., S-171 76 Stockholm, Sweden
SO Cancer Letters 106 (1). 1996. 91-96. ISSN: 0304-3835
LA English
AB Etoposide is extensively (approximately 94%) bound to plasma proteins and the free non-protein-bound levels have been shown to correlate more closely to toxicity than total drug concentrations. A rapid and easily performed method, compared to the time consuming equilibrium dialysis, to obtain the free fraction is needed. The aim of this study was to evaluate ultrafiltration and subsequent high performance liquid chromatography (HPLC) for the determination of protein binding of etoposide. Spiked plasma from healthy, drug-free volunteers was used to compare ultrafiltration, using Amicon Centrifree filters, with equilibrium dialysis at 37 degree C. The variability (CV) of the ultrafiltration method was 6.1 and 13.5% (n = 6) at 37 degree C and room temperature (RT), respectively. The relative size of the free fraction obtained by ultrafiltration at 37 degree C and RT was 1.22 (P = 0.0005) and 0.37 (P = 0.0001), respectively, compared with equilibrium dialysis at 37 degree C. The chromatographic separation of metabolites from the mother compound when free etoposide is analyzed is crucial. It is shown that a hydroxyacid metabolite of etoposide is quite dominant in a protein-free plasma fraction. The free concentrations were determined throughout a dose interval of 24 h in a patient receiving etoposide 100 mg/m-2 daily. Ultrafiltration and subsequent HPLC is considered convenient and suitable for in vivo pharmacokinetic investigations.

L9 ANSWER 8 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 1
AN 96:158364 BIOSIS
DN 98730499
TI Partial N-terminal amino acid sequence of the anti-neoplastic urinary protein (**ANUP**) and the anti-tumour effect of the N-terminal nonapeptide of the unique cytokine present in human granulocytes.
AU Ridge R J; Sloane N H
CS Anti-tumor Res. Products, Inc., 1842 Brookside Drive, Germantown, TN 38138, USA
SO Cytokine 8 (1). 1996. 1-5. ISSN: 1043-4666
LA English
AB The N-terminal amino acid sequence of the anti-neoplastic urinary protein (**ANUP**), a unique cytokine present in human granulocytes, was determined to be: Pyroglu-Leu-Lys-X-Tyr-Thr-X-Lys-Glu-Pro-Met-Thr-Ser(Thr)-Ala-Ala...This sequence showed no significant homology with any other protein when used in database searches. Furthermore, a synthetic nonapeptide corresponding to the first nine residues, with Cys in positions 4 and 7, was found to be a biologically active in vitro anti-tumour agent. An alternate method for the purification of **ANUP** to that previously reported is also presented. This method involves differential Amicon Diaflo membrane filtration.

L9 ANSWER 9 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS

AN 96:247573 BIOSIS
DN 98803702
TI Evaluating the ability of a potent anticancer agent, adozelesin (U-73975), to induce expression of stress genes in the xenometrics Pro-Tox (C), CAT-Tox (L), and CAT-Tox D assays.
AU Aaron C S; Marks T A
CS Upjohn Co., Kalamazoo, MI, USA
SO 27th Annual Scientific Meeting of the Environmental Mutagen Society, Victoria, British Columbia, Canada, March 23-28, 1996. Environmental and Molecular Mutagenesis 27 (SUPPL. 27). 1996. 1. ISSN: 0893-6692
DT Conference
LA English

L9 ANSWER 10 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 95:186142 BIOSIS
DN 98200442
TI Demonstration of Rb-mediated drug sensitivity and growth inhibition by an inducible expression system.
AU Fan J; Li W W; Bujard H; Bertino J R
CS Meml. Sloan-Kettering Cancer Cent., New York, NY 10021, USA
SO Eighty-sixth Annual Meeting of the American Association for Cancer Research, Toronto, Ontario, Canada, March 18-22, 1995. Proceedings of the American Association for Cancer Research Annual Meeting 36 (0). 1995. 329. ISSN: 0197-016X
DT Conference
LA English

L9 ANSWER 11 OF 30 USPATFULL DUPLICATE 2
AN 94:26632 USPATFULL
TI Parital primary amino acid sequence of the **antineoplastic protein** (**ANUP**); a cytokine present in granulocytes
IN Sloane, Nathan H., 1842 Brookside Dr., Germantown, TN, United States 38138
PI US 5298604 940329
AI US 93-116539 930902 (8)
RLI Continuation of Ser. No. US 92-919885, filed on 27 Jul 1992
DT Utility
EXNAM Primary Examiner: Schain, Howard E.
LREP Longacre & White
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 249
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Electrophoretically homogeneous human Antineoplastic Urinary Protein (**ANUP**) contains a blocked N-terminal amino acid that has been identified as pyroglutamic acid. Removal of the pyroglutamy residue by the use of pyroglutamyl aminopeptidose results in the formation of the deblocked protein which is also an antineoplastic molecule. The amino acid sequence of the deblocked **ANUP** 16 KD monomer showed the following sequence:

Cycle No.

1. Leu L

2. Lys K

3. Cys C

4. Tyr Y

5. Thr T

6. Cys C

7. Lys K

8. Glu E

9. Pro P

10. Met M

Cycle No.

11. Thr T

12. Thr (T)? or Ser (S)?

13. Ala A

14. Ala A

15. X?

A data base search using the above sequence showed that 100% homology with another protein was not found regardless of unassigned positions.

The blocked N-terminal amino acid of **ANUP** is pyroglutamic acid.

L9 ANSWER 12 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 94:164953 BIOSIS
DN 97177953
TI A new crystal form of abrin-a from the seeds of Abrus precatorius.
AU Tahirov T H O; Lu T-H; Liaw Y-C; Chu S-C; Lin J-Y
CS Dep. Physics, Natl. Tsing Hua Univ., Hsinchu 300 TAI
SO Journal of Molecular Biology 235 (3). 1994. 1152-1153. ISSN: 0022-2836
LA English
AB A new crystal form of abrin-a from the seeds of Abrus precatorius has been obtained by vapor diffusion method. The abrin-a crystals belong to monoclinic space group P2-1 with cell dimensions a = 84.58 ANG , b = 73.07 ANG , c = 48.23 ANG , beta = 96.20 degree C. An asymmetric unit contains one protein molecule of molecular weight 65 kDa and has a solvent content of approximately 46%.

L9 ANSWER 13 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 95:128488 BIOSIS
DN 98142788
TI Comparative studies on the anti-invasive effects of retinoic acid and staurosporine.
AU Popowicz P; Linder S
CS Div. Exp. Oncol., Dep. Gen. Oncol., Radiumhemmet, Karolinska Inst. Hosp., S-171 76 Stockholm, Sweden
SO Oncology Reports 1 (3). 1994. 529-532.
LA English
AB Retinoic acid and the protein kinase C inhibitor staurosporine have been reported to inhibit the invasiveness of tumor cells and may potentially be used to prevent metastatic disease. We report that retinoic acid reduced the invasiveness of 6 of 6 ras-transformed rat fibroblast cell lines and that inhibition did not require expression of the c-Jun component of AP-1. In contrast, staurosporine reduced the invasiveness of only 1 of 4 ras-transformed cell lines. The effect of staurosporine on the invasiveness of human tumor cell lines varied with cell type and length of treatment. We conclude that retinoic acid, but not necessarily staurosporine, decreases the

invasiveness of ras-transformed fibroblasts.

L9 ANSWER 14 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 3
AN 94:258134 BIOSIS
DN 97271134
TI Impaired bactericidal activity of PMN from two brothers with necrotizing ulcerative gingivo-periodontitis.
AU Cutler C W; Wasfy M O; Ghaffar K; Hosni M; Lloyd D R
CS Univ. Texas Health Sci. Center, Dep. Periodontology, P.O Box 20068, Houston, TX 77225, USA
SO Journal of Periodontology 65 (4). 1994. 357-363. ISSN: 0022-3492
LA English
AB The purpose of this study was to investigate the pathogenesis of necrotizing ulcerative gingivo-periodontitis (**ANUP**) diagnosed in two brothers, age 9 (ANUP1) and 14 (ANUP2) from rural Egypt. Complete blood count, differential and blood chemistry were within normal limits for both brothers and they were not malnourished. The phagocytosis and killing function of their polymorphonuclear leukocytes (PMN) towards four bacterial species were assessed using a fluorochrome microassay. The selection of bacterial species was based on preliminary microbiological results in early onset periodontitis in Egypt. Fluorochrome-labeled Prevotella intermedia, Peptostreptococcus micros, Campylobacter rectus, and Porphyromonas gingivalis were pre-opsonized with **ANUP** serum and added to PMN from both **ANUP** patients, as well as PMN from three sex-matched and two sex-and age-matched healthy Egyptian control (CTL) subjects. We found significant depressions (P lt 0.05) in PMN phagocytosis and killing of C. rectus and P. intermedia by ANUP1 and ANUP2, when compared to all CTL PMN. An assessment of the Gram-negative subgingival microflora present in both **ANUP** patients (in colony forming unit percent of total CFU recovered) (CFU%) revealed the presence of P. intermedia (ANUP1, 41.7 CFU%; ANUP2, 14.8 CFU%), Fusobacterium nucleatum (ANUP1, 3.6 CFU%; ANUP2, 48.1 CFU%), and Veillonella spp. (ANUP1, 18.2 CFU%; ANUP2, 18.5 CFU%). Spirochetes were also observed in cytocentrifuged, Gram-stained plaque from both **ANUP** patients. The predominant Gram-positive bacterial species recovered from both NUG1 and NUG2 was Streptococcus morbillorum.

L9 ANSWER 15 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 95:160056 BIOSIS
DN 98174356
TI Parenteral product development of AG337, a thymidylate synthase inhibitor.
AU Thirucote R; Laskin P; Chiang C-C; Tyle P
CS Agouron Pharm. Inc., 3565 General Atomics Court, San Diego, CA 92121, USA
SO European Journal of Pharmaceutics and Biopharmaceutics 40 (5). 1994. 271-276. ISSN: 0939-6411
LA English

L9 ANSWER 16 OF 30 USPATFULL
AN 93:107121 USPATFULL
TI Boronated phosphoramidate compounds
IN Spielvogel, Bernard F., 107 Wood Glen Dr., Cary, NC, United States 27511
Sood, Anup, 5041 Gatewood Dr., Durham, NC, United States 27712
PI US 5272250 931221
AI US 92-911218 920710 (7)
DT Utility
EXNAM Primary Examiner: Higel, Floyd D.
LREP Bell, Seltzer, Park & Gibson
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 814
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A class of pharmaceutically active boronated compounds are provided. The boronated compounds include boronated phosphoramidates, and boronated nucleosides, and oligomers thereof. The compounds are boronated by an aminoalkyl substituted polyborane, carborane, metallopolyborane or metallocarborane.

L9 ANSWER 17 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 94:64879 BIOSIS
DN 97077879
TI Crosstalk between epidermal growth factor receptor and P-glycoprotein in actinomycin D-resistant Chinese hamster lung cells.
AU Meyers M B; Yu P; Mendelsohn J
CS Lab. Cellular Biochemical Genetics, Memorial Sloan-Kettering Cancer Cent., 1275 York Ave., New York, NY 10021, USA
SO Biochemical Pharmacology 46 (10). 1993. 1841-1848. ISSN: 0006-2952
LA English
AB Multidrug-resistant cells can manifest an increase in epidermal growth factor (EGF) receptor number along with increased P-glycoprotein (Pgp) synthesis. An interrelationship of the two membrane proteins in actinomycin D-resistant Chinese hamster lung cells (DC-3F/AD X) in terms of the effect of EGF on Pgp phosphorylation was investigated. EGF was not a mitogen for the resistant cells, nor was it mitogenic for DC-3F, the parental drug-sensitive line. Brief treatment of DC-3F/AD X cells with EGF resulted in a 30-50% decrease in the level of Pgp phosphorylation, and treatment of the cells with okadaic acid, a specific inhibitor of protein phosphatases-1 and -2A (PP1 and 2A), increased Pgp phosphorylation. Okadaic acid also increased phosphorylation of Pgp in plasma membranes isolated from DC-3F/AD X cells by 30-40%. Protein phosphatase activity in extracts of cells grown in EGFcontaining medium was greater by 30% than that of cells grown in standard medium, and okadaic acid inhibited the increases. The results suggested that EGF activated PP1 and PP2A in DC-3F/AD X cells and that Pgp was a substrate for the phosphatases. The properties of Pgp may be modulated by the signalling system transduced by ligand-activated EGF receptor.

L9 ANSWER 18 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 93:358880 BIOSIS
DN BR45:42305
TI NONCORRELATION BETWEEN INTRINSIC CISPLATIN SENSITIVITY AND THE LEVELS OF A PANEL OF HEAT SHOCK PROTEINS 27 60 72 73 AND 90 IN HUMAN CELL LINES.
AU HETTINGA J V E; MEIJER C; MULDER N H; KONINGS A W T; DE VRIES E G E; KAMPINGA H H
CS DEP. RADIOBIOL., UNIV. GRONINGEN, GRONINGEN.
SO 84TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, ORLANDO, FLORIDA, USA, MAY 19-22, 1993. PROC AM ASSOC CANCER RES ANNU MEET 34 (0). 1993. 24. CODEN: PAMREA
DT Conference
LA English

L9 ANSWER 19 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 91:264867 BIOSIS
DN BR40:127747
TI ANTITUMOR PROTEINS IN MILK AND MILK WHEY RELATED TO THE HUMAN ANTINEOPLASTIC URINARY PROTEIN **ANUP**.
AU SLOANE N H; STEVENS S E JR
CS DEP. BIOL., MEMPHIS STATE UNIV., MEMPHIS, TENN. 38152.
SO 75TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ATLANTA, GEORGIA, USA, APRIL 21-25, 1991. FASEB (FED AM SOC EXP BIOL) J 5 (4). 1991. A546. CODEN: FAJOEC ISSN: 0892-6638

DT Conference
LA English

L9 ANSWER 20 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 4
AN 90:517377 BIOSIS
DN BA90:134653
TI ANALYSIS OF THE SUBSTRATE BINDING SITES OF HUMAN GALACTOSYLTRANSFERASE BY PROTEIN ENGINEERING.
AU AOKI D; APPERT E; JOHNSON D; WONG S S; FUKUDA M N
CS LA JOLLA CANCER RES. FOUND., LA JOLLA, CALIF. 92037.
SO EMBO (EUR MOL BIOL ORGAN) J 9 (10). 1990. 3171-3178. CODEN: EMJODG ISSN: 0261-4189
LA English
AB An expression vector, pIN-GT, encoding the soluble form of .beta.1,4-galactosyltransferase (GT) has been constructed from human GT cDNAs and the pIN-III-ompA2 expression vector. Escherichia coil strain SB221 harboring the pIN-GT plasmid produces and secretes a fusion protein consisting of the ompA signal and GT. The expression of GT was detected by assaying enzymatic activity as well as by Western blotting using anti-GT antibodies. The recombinant GT was purified to homogeneity by N-acetylglucosamine-Sepharose affinity chromatography. The NH2-terminal peptide sequence of purified GT confirmed the cleavage site of the fusion protein by bacterial signal peptidase. This expression system was utilized to produce mutant forms of GT in order to identify specific amino acids involved in substrate binding sites. Photoaffinity labeling of GT with UDP-galactose analog, 4-azido-2-nitrophenyluridylylpyrophosphate (**ANUP**), followed by cyanogen bromide (CNBr) cleavage revealed that **ANUP** bound to a fragment of GT composed of amino acid residues from Asp276 to Met328. Within this peptide segment, Tyr284, Tyr287, Tyr309, Trp310 and Trp312 were separately substituted into Gly and Tyr287 into Phe by site-directed mutagenesis. Enzymatic activity assay showed drastic reduction of the activity in all of the mutants except that Tyr287 .fwdarw. Phe remained as active as wild-type GT. Kinetic studies of the mutated GT showed that Tyr284, Tyr309 and Trp310 are critically involved in the N-acetyglucosamine binding and Tyr309 involved in UDP-galactose binding as well. These results indicate that these tyrosines and tryptophans in GT are essential for the binding of the acceptor N-acetylglucosamine, and that UDP-galactose also binds to residue(s) nearby where N-acetylglucosamine binds.

L9 ANSWER 21 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 5
AN 90:132876 BIOSIS
DN BA89:71687
TI PURIFICATION AND CHARACTERIZATION OF AN ANTIBACTERIAL AND **ANTINEOPLASTIC PROTEIN** SECRETION OF A SEA HARE APLYSIA-JULIANA.
AU KAMIYA H; MURAMOTO K; GOTO R; SAKAI M; ENDO T; YAMAZAKI M
CS SCH. FISH. SCI., KITASATO UNIV., SANRIKU, IWATE 022-01, JPN.
SO TOXICON 27 (12). 1989. 1269-1278. CODEN: TOXIA6 ISSN: 0041-0101
LA English
AB The fetid secretion of a sea hare, Aplysia juliana, was lethal to crabs and also inhibited the growth of bacteria. When the secretion was partitioned between water and n-hexane, only the n-hexane layer, which had a nauseating odor, was lethal to crabs. The water-soluble fraction showed strong antibacterial activity and inhibited the growth of both Gram-positive and Gram-negative bacteria. Antibacterial activity of the water-soluble fraction was destroyed by heating at 50.degree.C for 15 min, but was resistant to treatment with proteolytic enzymes. The active principle, named julianin-S, was purified by gel filtration and ion exchange chromatography. The purified specimen gave a single protein showing a mol. wt of approximately 67,000, as determined by gel filtration. Julianin-S inhibited the growth of Bacillus subtilis by 50% at a concentration

of 70 ng protein/ml. It was also cytotoxic to murine tumor cells and inhibited in vitro growth of L1210 cells by 50% at a concentration of 8 ng protein/ml.

L9 ANSWER 22 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 89:162621 BIOSIS
DN BA87:84722
TI STUDIES ON BIOACTIVE COMPOUNDS 13. SYNTHESIS AND LACK OF GROWTH-INHIBITORY PROPERTIES OF CYCLOHEXANE-1 2 4-TRIOL 1 2-DIESTERS WHICH RESEMBLE RING C OF THE PHORBOL ESTER MOLECULE.
AU LAUGHTON C A; DALE I L; GESCHER A
CS CANCER RES. CAMPAIGN EXPERIMENTAL CHEMOTHERAPY GROUP, PHARM. SCI. INST., ASTON UNIV., ASTON TRIANGLE, BIRMINGHAM B47 ET, U.K.
SO J MED CHEM 32 (2). 1989. 428-433. CODEN: JMCMAR ISSN: 0022-2623
LA English
AB It has been suggested that ring C of biologically active phorbol esters is an essential structural feature of the pharmocophore which confers activity on these compounds. In this study the hypothesis has been tested that compounds which resemble ring C of the phorbol ester molecule mimic the ability of phorbol esters to inhibit cell growth at nontoxic concentrations. All four diastereoisomers of (.+-.)-1,2-di-O-octanoylcyclohexane-1,24-triol have been prepared from cyclohexen-4-ol and tested for growth-inhibitory and cytotoxic properties. The phorbol ester 12-O-tetradecanoylphorbol 13-acetate inhibited the growth of A549 human lung carcinoma cells by 50% at a concentration of 0.2 nM and exerted cytotoxicity at concentrations of > 1 .mu.M. Diacylglycerols are the physiological ligands and activators of protein kinase C, the receptor via which phorbol esters are thought to mediate their effects. The diacylglycerols 1-oleoyl-2-acetylglycerol and 1,2-dioctanoylglycerol and the cyclohexanetriol diesters inhibited the growth fo A549 cells only at concentrations of 10-5 to 10-4 M, at which they were also cytotoxic. A computer-assisted analysis of the goodness of fit between the cyclohexanetriol diesters and ring C of the phorbol moiety revealed possible energetic grounds for conformational dissimilarities. The results suggest that activation of protein kinase C alone is probably not sufficient to reproduce phorbol ester induced growth arrest in A549 cells and that the cyclohexanetriol diesters may lack pivotal elements of the phorbol ester pharmacophore.

L9 ANSWER 23 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 87:311050 BIOSIS
DN BR33:32723
TI EVIDENCE FOR THE INTERNALIZATION OF THE ANTINEOPLASTIC URINARY PROTEIN **ANUP**.
AU STRUVE W; CROCKER D; SLOANE N
CS UNIV. TENNESSEE, MEMPHIS, TENNESSEE 38163.
SO 78TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, PHILADELPHIA, PENNSYLVANIA, USA, JUNE 7-11, 1987. FED PROC 46 (6). 1987. 1989. CODEN: FEPRA7 ISSN: 0014-9446
DT Conference
LA English

L9 ANSWER 24 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 87:370361 BIOSIS
DN BR33:60836
TI RELATIONSHIPS BETWEEN DRUG-INDUCED TOPOISOMERASE II-MEDIATED DNA DAMAGE AND DNA REPLICATION IN SYNCHRONIZED 3T3 CELLS.
AU COVEY J M; KOHN K W; POMMIER Y
CS LAB. MOLECULAR PHARMACOLOGY, NCI, NIH, BETHESDA, MD. 20892.
SO SEVENTY-EIGHTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, ATLANTA, GEORGIA, USA, MAY 20-23, 1987. PROC AM ASSOC CANCER RES ANNU MEET 28 (0). 1987. 267. CODEN: PAMREA
DT Conference
LA English

L9 ANSWER 25 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 6
AN 86:222285 BIOSIS
DN BA81:113585
TI STUDIES ON AN ANTINEOPLASTIC FRACTION FROM HUMAN URINE CHARACTERIZATION OF THE MAJOR PROTEIN IN THIS FRACTION.
AU SLOANE N H; LYNN W R; MACLEOD R M; HADE E P K; POTTATHIL R; KYRIAZIS A P
CS DEP. BIOCHEM., UNIV. TENNESSEE COLL. MED., MEMPHIS, TENN. 38163, USA.
SO BIOCHEM J 234 (2). 1986. 355-362. CODEN: BIJOAK ISSN: 0306-3275
LA English
AB A fraction had been isolated from human urine which exhibits antiproliferative activity against human tumour cell lines without affecting the growth of several normal diploid cell lines or tumour cells of mouse or hamster origin. The major protein present in this fraction has been characterized and tentatively designated antineoplastic urinary protein (**ANUP**). An S020,W value of 3.69 S was obtained by sedimentation velocity analysis, and a subunit molecular mass of 16300 Da was obtained by sedimentation equilibrium and by sodium dodecyl sulphate/polyacrylamide-gel electrophoresis. Centrifugation data also indicated that the protein self-associates. The amino acid analysis of **ANUP** was consistent with its low pI (4.2) as determined by chromatofocusing analysis. Furthermore, the amino acid composition exhibited some features similar to collagen, as shown by high levels of proline and glycine, the absence of cysteine, and the presence of low levels of hydroxyproline.

L9 ANSWER 26 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 86:256556 BIOSIS
DN BA82:11305
TI RADIOMETRIC EVALUATION OF ANTIBACTERIAL ACTIVITY OF BOUVARDIN NSC-259968 ON ESCHERICHIA-COLI AND STAPHYLOCOCCUS-AUREUS.
AU BASRUR V S; CHITNIS M P; MENON R S
CS CELLULAR CHEMOTHERAPY UNIT, CANCER RES. INST., TATA MEMORIAL CENTRE, PAREL, BOMBAY 400 012, INDIA.
SO INDIAN J EXP BIOL 24 (3). 1986. 156-158. CODEN: IJEBA6 ISSN: 0019-5189
LA English
AB Bouvardin, a cyclic hexapeptide and a new **antineoplastic, protein** synthesis inhibitor, was studied for its effects on bacterial growth and metabolism. E. coli and S. aureus as representative types of gram-negative and gram-positive bacteria respectively were used for these studies. Garamycin and kanamycin were also employed as known antibiotics to compare their effects with bouvardin. Both garamycin and kanamycin markedly reduced 14C-glucose metabolism at a concentration of 10 .mu.g/ml. However, bouvardin revealed no such antibacterial activity in these microorganisms.

L9 ANSWER 27 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 7
AN 84:217658 BIOSIS
DN BA77:50642
TI PHOTO AFFINITY LABELING OF LACTOSE SYNTHASE EC-2.4.1.22 WITH A UDP GALACTOSE ANALOG.
AU LEE T K; WONG L-J C; WONG S S
CS SIMON'S ROCK BARD COLL., GREAT BARRINGTON, MASS. 01230.
SO J BIOL CHEM 258 (21). 1983. 13166-13171. CODEN: JBCHA3 ISSN: 0021-9258
LA English
AB A photoaffinity analog of UDP-galactose, 4-azido-2-nitrophenyluridylyl pyrophosphate (**ANUP**), was synthesized for the investigation of the binding topography of [bovine milk] .alpha.-lactalbumin on galactosyltransferase [EC 2.4.1.38]. Results obtained from steady state kinetics show that **ANUP** is an effective competitive inhibitor against UDP-galactose in the reactions of lactose and N-acetyllactosamine syntheses. The specific

binding of **ANUP** to the UDP-galactose-binding site is further demonstrated by its ability to facilitate the formation of the lactose synthase complex on solid supports, either alone or in the presence of glucose or N-acetylglucosamine. **ANUP** inactivates galactosyltransferase on irradiation. One mole of **ANUP** was incorporated per mol of enzyme inactivated. This process is Mn2+-dependent and can be prevented by UDP-galactose. Glucose and N-acetylglucosamine render only partial protection. Photoaffinity labeling of lactose synthase either free in solution or immobilized on Sepharose does not result in any reduction of the .alpha.-lactalbumin modifer activity. In addition, no incorporation of radioactivity into .alpha.-lactalbumin was observed when radioactive **ANUP** was used, whereas galactosyltransferase was labeled. .alpha.-Lactalbumin does not bind to galactosyltransferase in the region of the **ANUP** site, suggesting that the location of protein-protein interaction between the 2 subunits of lactose synthase may be removed from the UDP-galactose-binding domain.

L9 ANSWER 28 OF 30 USPATFULL
AN 82:55614 USPATFULL
TI Isolation of an **antineoplastic protein** fraction and an antineoplastic peptide fraction from human urine
IN Sloane, Nathan H., Germantown, TN, United States
PA University of Tennessee Research Corporation, Knoxville, TN, United States (U.S. corporation)
PI US 4359415 821116
AI US 81-269995 810603 (6)
DT Utility
EXNAM Primary Examiner: Lieberman, Allan; Assistant Examiner: Short, P.
LREP Luedeka, Fitch & Neely
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 230
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The passage of human urine through a bed of adsorbent material results in the adsorption from the urine of antineoplastic substances as determined by in vitro tissue culture techniques utilizing human tumor cells. The adsorbent yields two antineoplastic fractions upon sequential elution. Elution of the low-molecular weight antineoplastic fraction is accomplished by elution with cold aqueous acetone at slightly alkaline pH. Thereafter, elution of the high molecular weight antineoplastic fraction is accomplished by elution with a cold aqueous acetone-glycerol mixture at slightly alkaline pH.

The antineoplastic activities of these fractions are determined by tissue culture techniques employing a variety of human neoplastic cells. Furthermore, the high molecular weight fraction, the antineoplastic urinary protein, also inhibits the progression and causes regression of certain human tumor cells implanted in the nude mouse.

L9 ANSWER 29 OF 30 BIOSIS COPYRIGHT 1998 BIOSIS
AN 78:222765 BIOSIS
DN BA66:35262
TI CESALIN AN ANTI NEOPLASTIC PROTEIN.
AU MONTGOMERY R; YAMAUCHI F; BRADNER W T
CS DEP. BIOCHEM., UNIV. IOWA, IOWA CITY, IOWA 52242, USA.
SO LLOYDIA (CINCI) 40 (3). 1977 269-274. CODEN: LLOYA2 ISSN: 0024-5461
LA English
AB An **antineoplastic protein** was isolated from the endosperm of the seeds of Caesalpinia gilliesii by extraction with water, dialysis and precipitation by ammonium sulfate or

acidification. The precipitated protein mixture was separated by column chromatography into 3 proteins, 1 of which, termed cesalin, inhibited the growth of Walker 256 carcinosarcoma. There is an associated carbohydrate with the cesalin that can be largely removed by chromatography on hydroxylapatite. The remaining carbohydrate (about 0.3%) is a hexosan. Cesalin, MW 110,000, migrates as a single component by polyacrylamide gel electrophoresis at pH 8.3 but in a denaturing system containing sodium dodecyl sulfate, 3 bands were observed. These correspond to protein subunits of approximately 30,000 daltons. Antitumor tests in rats showed 70-80% inhibition of Walker 256 growth at a dose of 80 .mu.g/kg per day of cesalin.

L9 ANSWER 30 OF 30 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 72-09532T [06] WPIDS
TI Aluminium sodium ultraphosphate - for chelating metal ions.
DC E33
PA (KOR-I) KORYO J
CYC 1
PI JP 47004041 B (7206)*
PRAI JP 69-53348 690704
AB JP72004041 B UPAB: 930000
Al (0.04 - 0.01 mol) or Al2O3 (0.04 - 0.2 mol) is added to Na ultraphosphate (NUP) (1 mol), or to the mixture (1 mol), consisting of phosphoric acid and NaOH or NaCO3 and the title cpd. (**ANUP**) is prepd. by melting them at 750 - 900 degrees C, and cooling rapidly. The soln. velocity of **ANUP** to water is far slower than NUP. Hygroscopicity of **ANUP** is markedly smaller than NUP.

=> d his

(FILE 'HOME' ENTERED AT 14:57:58 ON 20 AUG 1998)

FILE 'REGISTRY' ENTERED AT 14:58:06 ON 20 AUG 1998
L1 0 S XLKCYTCKQPMTSAAC/SQEP
L2 0 S XLKCYTCKEPMTSAAC/SQEP
L3 0 S (ANTINEOPLASTIC PROTEIN OR ANUP)/CN
L4 0 S QLKCYTCKQPMTSAAC/SQEP
L5 0 S XLKCYTCKXPMTSAAC/SQEP

FILE 'CA' ENTERED AT 15:13:31 ON 20 AUG 1998
L6 16 S (ANTINEOPLASTIC PROTEIN OR ANUP)/BI,AB

FILE 'BIOSIS, MEDLINE, EMBASE, USPATFULL, WPIDS' ENTERED AT 15:20:41 ON 20 AUG 1998
L7 41 S L6

FILE 'CA' ENTERED AT 15:21:47 ON 20 AUG 1998
L8 16 DUP REM L6 (0 DUPLICATES REMOVED)

FILE 'BIOSIS, MEDLINE, EMBASE, USPATFULL, WPIDS' ENTERED AT 15:22:29 ON 20 AUG 1998
L9 30 DUP REM L7 (11 DUPLICATES REMOVED)